

## CLAIMS

1. A method for ameliorating neuronal atrophy and loss accompanying normal aging in the mammalian brain, the method comprising delivering a unit dosage of a growth factor-encoding transgene composition to preselected delivery sites in the brain, wherein the encoded growth factor is expressed in the brain, and stimulates axonal growth in targeted growth factor-receptive neurons therein.

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2. The method according to Claim 1, wherein the targeted growth factor-receptive neurons are cholinergic neurons.

10 3. The method according to Claim 2, wherein the targeted cholinergic neurons are within 550 µm of a delivery site, and wherein further growth is stimulated in said neurons by the expressed growth factor.

4. The method according to Claim 2, wherein terminal axons of targeted cholinergic neurons are located more than 550 µm from a delivery site, and wherein further growth is

15 stimulated in said terminal axons by the expressed growth factor.

5. The method according to Claim 1, wherein the growth factor-encoding transgene composition is delivered in vivo, by introduction of a transgene-expressing recombinant expression vector into the brain.

6. The method according to Claim 1, wherein the growth factor-encoding transgene

20 composition is delivered ex vivo, from grafts of transgene-secreting donor cells introduced into the brain.

7. The method according to Claim 5, wherein the transgene-expressing recombinant expression vector is a viral vector.

8. The method according to Claim 7, wherein the viral vector is delivered in a pharmaceutically acceptable composition, and provides from  $10^{10}$  to  $10^{12}$  viral particles/ml of composition.

9. The method according to Claim 6, wherein the donor cells are delivered in a 5 pharmaceutically acceptable composition having a concentration of at least  $1 \times 10^5$  donor cells/ $\mu$ l.

10. The method according to Claim 9, wherein each graft contains from 2 to 20  $\mu$ l of the donor cell containing composition.

11. The method according to Claim 1, wherein the mammal is a human and the 10 transgene encodes a human nervous system growth factor.

12. The method according to Claim 11, wherein the transgene encodes nerve growth factor (NGF).

13. The method according to Claim 11, wherein the transgene encodes neurotrophin 3 (NT-3).

15 14. The method according to Claim 1, wherein the delivery cell sites are all within the Ch4 region of the cholinergic basal forebrain.

15. The method according to Claim 1, wherein each delivery site is preselected by correlating loss of cortical fiber density to impairment of neurological function in the aging brain.